

## Remarks

Applicants have amended claims as shown supra. Applicants provide herewith Table 1, wherein the specific support for the amended claims is indicated. Table 1 is attached herewith as an Exhibit A.

Applicants also introduce a set of new claims 39-48. Support for the new claims is shown in Table 2. Table 2 is attached herewith as an Exhibit B.

Accordingly, Applicants respectfully submit that neither the claim amendments nor the new claims introduce new matter and request that both the amendments and the new claims be entered.

Claims 30-33, and 36-38 have been cancelled without prejudice.

Applicants now turn to the specific rejections.

The Examiner rejected claims 11, 24-26, and 30-38 as allegedly not complying with 35 U.S.C. §112, first paragraph, written description requirement. Specifically, the Examiner alleged that the specification does not describe **“that each copy has an identical generic oligonucleotide that is attached to the array’s x and y coordinates.”** (Page 4, lines 14-17 of the 5/28/08 Office Action.)

Applicants respectfully disagree. At page 10, lines 10-15, the specification reads that the “method contemplates a **solid support with positions for oligonucleotides defined by x and y coordinates**. At each position ... a **oligonucleotide is immobilized**. In one embodiment... the **same oligonucleotide** (i.e., an oligonucleotide with the **same generic nucleotide** sequence) is **immobilized in every position.**” (Emphasis added)

Applicants have amended the claims to change the term “identical” to term “same.” With this amendment, the specification provides *verbatim* support for this claim.

As described in the method of making these arrays, the oligonucleotides serve as an “anchor” to attach the multiple copies of the unique target nucleic acids to the solid surface. As explained in the specification the “invention contemplates solving both problems [inconvenience of synthesizing long oligonucleotides and limited space in the x/y plane of any solid surface] by utilizing circular nucleic acid in the production of the array” (page 10, lines 10-11), the





two copies of said unique sequence of interest extending in the z dimension by the circular DNA template having the unique sequence of interest'

To expedite prosecution, Applicants have amended claims as shown above to address alleged lack of clarity.

Moreover, the Examiner rejected claim 11 alleging that because the preamble of the claim requires that between each unique sequence of the interest there is at least one region that is complementary to at least a portion of the identical generic oligonucleotide and

**“does not require that the at least a portion of the identical generic oligonucleotide is attached to the array defined by x and y coordinates from z coordinate,** if at least one region that is fully complementary to at least a portion of the identical generic oligonucleotide attached to the array's x and y coordinates and the identical generic oligonucleotide is attached to the array by a chemical bond from x or y coordinate, multiple copies of a sequence interest extend along either x or y dimension and does not extend along z dimension which is opposite to the claim.”

Applicants respectfully submit that the rejection be withdrawn for the following reasons.

As described in the specification (e.g., paragraph bridging pages 10 and 11), the array components for an embodiment claimed in claim 11 are as follows:

1. Solid surface wherein location of each nucleic acid sequence or “probe” can be defined using x and y coordinates; and
2. A plurality of nucleic acid sequences or a “probes” that are attached to the solid surface, wherein the “probe” has essentially three “parts”:
  - a. a nucleic acid sequence part that attaches the nucleic acid sequence to the solid surface (same for each of the nucleic acids sequences), this part also serves as a “primer” for the rolling circle;
  - b. a nucleic acid sequence part that corresponds to a unique target sequence - this part is repeated two or more times in the immobilized “probe”; and

- c. a nucleic acid sequence part that separates each copy of the unique target sequence and that is identical to at least part of the “primer” sequence - this sequence is introduced to the “probe” by the rolling circle method because the circular template used for the primer extension has to hybridize to the immobilized “primer.”

Applicants have amended the claims to make these components more explicit. In view of the amendments to claim 11, Applicants respectfully submit that the rejection be withdrawn.

The Examiner further rejected claim 23. Specifically, the Examiner asked “why the different unique sequence of the sequence of interest in the sequence of interest can be complementary to itself” (page 7, last two lines of the 5/28 Office Action).

Applicants respectfully submit that the rejection be withdrawn for the following reasons.

As described in the specification, for example in paragraph bridging pages 11 and 12, the array components for an embodiment claimed in claim 23 are as follows:

1. Solid surface wherein location of each nucleic acid sequence or “probe” can be defined using x and y coordinates; and
2. A plurality of nucleic acid sequences or a “probes” that are attached to the solid surface, wherein the “probe” has essentially three “parts”:
  - a. a nucleic acid sequence part that attaches the “probe” to the solid surface (different for each probe), this part also serves as a “primer” for the rolling circle and therefore, in this embodiment, this “primer” must be complementary to the unique sequence that is present in the circular template used to make the array;
  - b. a nucleic acid sequence part that corresponds to a unique target sequence - this part is repeated two or more times in the immobilized “probe”; and
  - c. a nucleic acid sequence part that separates each copy of the unique target sequence and that is identical to at least part of the “primer” sequence - this sequence is introduced to the “probe” by the rolling circle method because the



That is because the “separating region” has a sequence that is at least partially complementary to the “primer sequence” attaching the nucleic acid “probe” to the solid surface. However, because each of the sequence of interest or “target” that is repeated in the concatamer “probe” is different, each of the probes attached to the solid support is necessarily different.

In contrast, Smith teaches an array has the same trinucleotide repeat sequence repeated between two constant “primer” regions. The trinucleotide repeats are not separated by a “separating region.”

The Examiner appeared to argue that in claim 30 this distinction is not claimed because “claim 30 does not require that the unique sequence of interest is different from the generic nucleic acid sequence” (page 11, lines 15-16 of the May 28, 2008 Office Action).

Applicants respectfully submit that this requirement is clear in claim 39. The fact that each of the “primer” attachment parts is identical between all the “probes” and each of the “separating sequences” are at least partially complementary to the “primer” sequence makes it impossible for the “primer” and the “target” to be identical. Therefore the unique sequence of interest is necessarily different from the generic nucleic acid sequence.

The difference is also evident from the significant difference in the function between the Smith array and the presently claimed array. Smith array is designed to detect the length of a trinucleotide repeat for diagnostic purposes, whereas the present arrays are directed to detect the number or amount of a certain target sequence in a nucleic acid sample.

In other words, in the array of Claim 39, each immobilized nucleic acid is unique and comprises a identical sequence segment attached to the array (Segment 1) followed by repeats of the sequence complementary to the unique target sequence (Segment 2) and the sequence segment that is at least partially complementary to the identical sequence segment (Segment 3). Hence, as shown in Figure 2, in one embodiment, the probe can be depicted as:

**Segment 1-Segment 2- Segment 3-Segment 2- Segment 3-Segment 2- Segment 3...**

In contrast, as illustrated in Figure 1, in the arrays of Smith, each probe can be depicted as: **Segment-A –Segment-B–Segment-B–Segment-B–...Segment-C.**

Claim 46 is directed to an array of unique immobilized nucleic acid sequences wherein **each** unique immobilized nucleic acid sequence comprises two main sequence segments,

namely, a sequence segment that is different for each immobilized nucleic acid sequence and attached to the solid support (Segment-1), and a sequence segment (Segment-2), following the attached sequence segment, that is complementary to a sequence of interest, is different for each immobilized nucleic acid sequence, and is more than 13 nucleotides long

The sequence segment that is complementary to a target sequence is repeated at least two times.

In contrast, the Smith arrays have an identical “primer” sequence (Segment-A) attaching the trinucleotide repeat “probes” onto the solid support, and the trinucleotide repeats (Segment-B) are followed by an identical 3’ sequence (Segment-C), which is different from the 5’ attaching sequence (Segment-A) and corresponds to a region that flanks the trinucleotide repeat in the target nucleic acid. A schematic description of an array of Smith is depicted in Figure 1.

Thus, in the arrays of Claim 46, each immobilized nucleic acid is unique and comprises a unique sequence segment attached to the array (Segment 1) and is followed by repeats of the sequence complementary to the target sequence (Segment 2). Hence, in one embodiment, the probe can be depicted as: **Segment 1-Segment 2-Segment 2- Segment 2...** A schematic illustration of one embodiment of the arrays of Claim 46 is further illustrated in Figure 3. In contrast, in the arrays of Smith, shown in Figure 1, each probe can be depicted as: **Segment-A – Segment-B – Segment-B – Segment-B - Segment-C.**

Accordingly, Smith cannot anticipate claim 46.

Claim 50 is directed to an array of immobilized nucleic acid sequences wherein each of the “probes” are attached to the solid support by hybridization to a “primer” that has been attached to the solid surface. A schematic illustration of an embodiment of the arrays of Claim 50 is depicted in Figure 4.

As illustrated in Figure 1, Smith does not describe arrays, wherein the trinucleotide-repeat containing “probes” are attached to a solid surface by at least partially hybridizing the 5’ flanking sequence to a complementary “primer” attached to the solid surface,.

Accordingly, Smith cannot anticipate claim 50.

Application No.: 09/886,779  
Office Action mailed May 28, 2008  
Amendment filed November 26, 2008  
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In view of the foregoing, Applicants respectfully submit that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the Commissioner is authorized to charge Nixon Peabody LLP Deposit Account No. 50-0850.

Date: November 26, 2008

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